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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/905,810	07/13/2001	Paul Rennert	A068 US	6397

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EXAMINER
HADDAD, MAHER M

ART UNIT	PAPER NUMBER
1644	06

DATE MAILED: 08/27/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/905,810	RENNERT, PAUL	
	Examiner	Art Unit	
	Maher M. Haddad	1644	

-- The MAILING DATE of this communication appears on the cover sheet with th correspondence address --

P riod for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 July 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15* is/are pending in the application.

4a) Of the above claim(s) *6-9 and 15* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5 and 10-14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *12-03-01* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Claims 1-15 are pending.

2. Applicant's election with traverse of Group I, claims 1-15, drawn to a method for blocking the development or treating or reducing the severity or effects of an immunological disorder comprising administering an antibody directed against the TWEAK ligand graft-versus-host disease (GVDH) as the species, filed on 7-01-02, is acknowledged.

Applicant's traveral is on the grounds that Groups I-XV comprise claims that recite methods for using the biological properties of the interaction between the TWEAK ligand and its receptor, further, these groups all comprise claims that recite methods of administering a TWEAK blocking agent to a patient for the purpose of effecting inappropriate immunological activities. This is not found persuasive because different blocking agents employed in the methods are distinct because their structures are different and are therefore capable of separate manufacture, use and sale. Therefore, the methods of blocking the development or treating or reducing the severity or effects of an immunological disorder comprising administering specific antibodies/agents are distinct and independent, and searches of all groups would place an undue burden upon the examiner due to the distinct and divergent subject matter of each Group.

The requirement is still deemed proper and is therefore made FINAL.

Upon reconsideration Examiner has extended the species search to cover organ transplant failure resulting from graft rejection. Claims 1-5 and 10-14 read on the elected species.

3. Claims 6-9 and 15 are withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b) as being drawn to nonelected inventions.

4. Claims 1-5 and 10-14 are under examination as they read on a method for blocking the development or treating or reducing the severity or effects of an immunological disorder comprising administering an antibody directed against the TWEAK ligand wherein the immunological disorder is GVDH and organ transplant failure resulting from graft rejection.

5. The specification is objected to under 37 CFR 1.821(d) for failing to provide a sequence identifier for each individual sequence. Figure 1, on page 5, line 32 depicts two TWEAK sequences murine and human that each must have a sequence identifier. Correction is required.

6. Acknowledgment is made of applicant's claim for foreign priority based on an application filed in the United States on 01/14/2000. It is noted, however, that applicant has not filed a certified copy of the PCT/US00/01044 application as required by 35 U.S.C. 119(b).

7. The specification on page 1 should be amended to reflect the relationship of 60/116,168 and PCT application No. PCT/US00/01044 with the instant application.

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 1-5 and 10-14 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for blocking the development or treating or reducing the severity or effects in a subject having a graft-versus-host disease and organ transplant failure resulting from graft rejection comprising administering anti-TWEAK ligand monoclonal antibody does not reasonably provide enablement for a method for blocking the development or treating or reducing the severity or effects of **any immunological disorders** in an animal comprising the step of administering **any pharmaceutical composition** which comprises a therapeutically effective amount of **any TWEAK blocking agent** and a pharmaceutically acceptable carrier in claim 1; a method for inhibiting **any immune response** in an animal comprising the step of administering **any pharmaceutical** composition which comprises an effective amount of **any TWEAK blocking agent** and a pharmaceutically effective carrier in claim 2; wherein the TWEAK blocking agent is **any antibody directed against the TWEAK ligand** in claim 3(a); wherein the TWEAK blocking agent comprises **any monoclonal antibody directed against the TWEAK surface ligand**, in claim 10; wherein the antibody is directed against **any subunit of the TWEAK ligand** in claim 11; wherein the immune response is **any Th1 cell-mediated immune response** in claim 12, any **Th2 cell-mediated immune response** in claim 13 or **both any Th1 and any Th2 cell-mediated immune response** in claim 14. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The specification disclosure does not enable one skilled in the art to practice the invention without any undue amount of experimentation.

Besides anti-TWEAK monoclonal antibody, the specification fails to provide any guidance as to how to make and how to use any "TWEAK blocking agents", any "pharmaceutical composition", any "antibody directed against the TWEAK ligand", any "monoclonal antibody against TWEAK surface ligand" or any " antibody against any subunit of the TWEAK ligand" to treat any "immunological disorders" or inhibit any

"immune response" wherein the immune response is any "Th1 cell-mediated", "Th1 cell-mediated" or "both Th1 and Th2 mediated" immune response.

Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, the lack of sufficient working examples, the unpredictability in the art and the amount of experimentation required to enable one of skill in the art to practice the claimed invention.

Applicant has not provided sufficient biochemical information that distinctly identifies such "blocking agents" other than monoclonal antibodies against TWEAK ligand. While any "TWEAK blocking agent" may have some notion of the activity of the "inhibitory agent", claiming biochemical molecules by such properties fails to provide sufficient guidance and direction as to how the skilled artisan can make such agents, commensurate in scope with the claimed invention. The specification (page 16, lines 14-19) fails to provide any guidance on how to make any antibody against TWEAK ligand, any monoclonal antibody directed against the TWEAK surface ligand, any antibody against any subunit of the TWEAK ligand that can be used to treat a subject having a graft-versus-host disease and organ transplant failure resulting from graft rejection.

There is insufficient guidance as to which amino acid subunits within the TWEAK polypeptide can be unique and retain a distinct functional capability of the full length polypeptide. *In re Fisher*, 166 USPQ 18 indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. Since the amino acid sequence of a polypeptide determined its structural property, predictability of which amino acid subunit can retain the functional capabilities of the full length polypeptide requires knowledge of, and guidance with regard to, which segments in the polypeptide's sequence contribute to its function.

The current state of the art in antibody therapeutics and the predictability of treatment efficacy is complicated by the potential for antibody interactions with irrelevant or completing epitopes, Fc region engagement, reduced half life of antibody fragments, and immune response to the therapeutic antibodies (see Ward et al, pages 167-171, 1994 "consideration related to use of blocking antibodies"). Therefore, one skilled in the art at the time of the invention would not be able to predict which compounds such as antibodies will block immunological disorders or inhibit the immune response. Consequently the skilled artisan would not know how to use the instant invention as broadly claimed. While experimental testing techniques using surface ligand binding compounds are available, it is not routine in the art to use such methods when the expectation of success is unpredictable based on the instant disclosure. Thus, it would require an undue amount of experimentation of one skilled in the art to practice the invention as broadly claimed.

Therefore, there is insufficient direction or objective evidence as to how to make and to how to use any agent which inhibits any cadherin-11 activity for the number of possibilities associated with the myriad of direct and indirect effects associated with various "inhibitory agents" and, in turn, as to whether such a desired effect can be achieved or predicted, as encompassed by the claims.

10. Claims 1-5 and 10-14 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant is in possession of a method for blocking the development or treating or reducing the severity or effects in a subject having a graft-versus-host disease and organ transplant failure resulting from graft rejection comprising administering anti-TWEAK ligand monoclonal antibody.

Applicant is not in possession of any method for blocking the development or treating or reducing the severity or effects of any immunological disorders in an animal comprising the step of administering any pharmaceutical composition which comprises a therapeutically effective amount of any TWEAK blocking agent and a pharmaceutically acceptable carrier in claim 1; a method for inhibiting any immune response in an animal comprising the step of administering any pharmaceutical composition which comprises an effective amount of any TWEAK blocking agent and a pharmaceutically effective carrier in claim 2; wherein the TWEAK blocking agent is any antibody directed against the TWEAK ligand in claim 3(a); wherein the TWEAK blocking agent comprises any monoclonal antibody directed against the TWEAK surface ligand, in claim 10; wherein the antibody is directed against any subunit of the TWEAK ligand in claim 11; wherein the immune response is any Th1 cell-mediated immune response in claim 12, any Th2 cell-mediated immune response in claim 13 or both any Th1 and any Th2 cell-mediated immune response in claim 14.

Applicant has disclosed only anti-TWEAK antibody; therefore, the skilled artisan cannot envision all the contemplated TWEAK blocking agent possibilities recited in the instant claims. Consequently, conception cannot be achieved until a representative description of the structural and functional properties of the claimed invention has occurred, regardless of the complexity or simplicity of the method. Adequate written description requires more than a mere statement that it is part of the invention. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC1993). The Guidelines for the Examination of Patent Application Under the 35 U.S.C.112, ¶ 1"Written Description" Requirement make clear that the written description requirement for a claimed genus may be satisfied

through sufficient description of a representative number of species disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 20001, see especially page 1106 3rd column).

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.). Consequently, Applicant was not in possession of the instant claimed invention. See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.

Applicant is directed to the Revised Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

11. No claim is allowed.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maher Haddad, whose telephone number is (703) 306-3472. The examiner can normally be reached Monday to Friday from 8:00 to 4:30. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached at (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center

located in Crystal Mall 1. The faxing of papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Maher Haddad, Ph.D.
Patent Examiner
Technology Center 1600
August 26, 2002

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